

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20-262/S-024

ADMINISTRATIVE DOCUMENTS

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

NDA/BLA # 20-262

Supplement # 024 Circle one: SE1 SE2 SE3 SE4 SE5 SE6

HFD-150 Trade and generic names/dosage form: Taxol (paclitaxel) Injection Action: (AP) AE NA

Applicant Bristol-Myers Squibb Therapeutic Class CYTOTOXIC

Indication(s) previously approved: 1st-line treatment of advanced carcinoma of the ovary
breast cancer after failure of combination chemotherapy for metastatic disease or relapse ≥ 6 months of adjuv.
2nd-line AIDS-related Kaposi's sarcoma
1st-line therapy in combination w/ cisplatin in advanced ovarian carcinoma

Pediatric information in labeling of approved indication(s) is adequate ☒ inadequate

Proposed indication in this application use in combination w/ asplatin for the treatment of non-small cell lung cancer in patients who are not candidates for potentially curative surgery

FOR SUPPLEMENTS, ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.
IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS?

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply) ☐ Yes (Continue with questions) ☒ No (Sign and return the form)

___ Neonates (Birth-1month) ___ Infants (1month-2yrs) ___ Children (2-12yrs) ___ Adolescents(12-16yrs)

— 1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for all pediatric age groups. Further information is not required.

— 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

— 3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

 a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

___ b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

___ c. The applicant has committed to doing such studies as will be required.

— (1) Studies are ongoing,

— (2) Protocols were submitted and approved.

— (3) Protocols were submitted and are under review.

— (4) If no protocol has been submitted, attach memo describing status of discussions.

— d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

— 4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

— 5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? Yes No
ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from /S/ (e.g., medical review, medical officer, team leader)

Signature of Preparer and Title

cc: Orig NDA/BLA # 20-262
HFD-150 / Div File / D. Spillman
NDA/BLA Action Package
HFD-006/ KRoberts

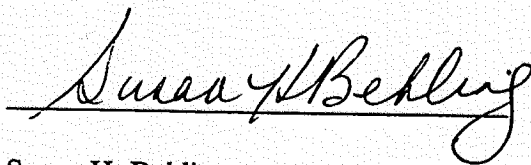
FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-6 (ROBERTSK)

(revised 10/20/97)

CERTIFICATION: DEBARRED PERSONS

This certifies that Bristol-Myers Squibb Company has not used in any capacity any persons identified by the United States Food and Drug Administration on the April 8, 1997 Debarment List, as well as any persons identified as being debarred in the Federal Register through June 1, 1997.

Further, we certify that Bristol-Myers Squibb Company will not use the services in any capacity of anyone debarred by the United States Food and Drug Administration.



Date: 6/20/97

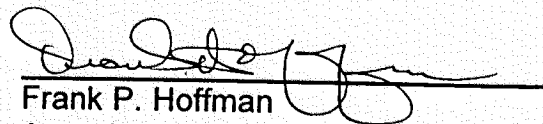
Susan H. Behling
Associate Director, Worldwide Regulatory Affairs
Bristol-Myers Squibb Company
5 Research Parkway
P.O. Box 5100
Wallingford, CT 06447-7660
(203) 284-7593

PATENT INFORMATION CERTIFICATION

The undersigned declares that U.S. Patent Nos. 5,641,803 and 5,670,537 cover the use of TAXOL® (paclitaxel) at a dose of about 175 mg/m² given intravenously over about 3 hours for the treatment of non-small cell lung cancer.

This product is currently approved under Section 505 of the Federal Food, Drug and Cosmetic Act.

Dated: March 10, 1998

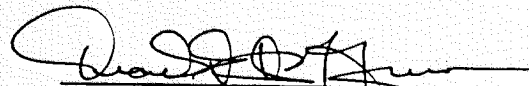


Frank P. Hoffman
Associate Patent Counsel
Bristol-Myers Squibb Co.

PATENT INFORMATION CERTIFICATION

The undersigned declares that U.S. Patent No. 5,641,803 covers the use of TAXOL® (paclitaxel) at a dose of about 175 mg/m² given intravenously over about 3 hours for the treatment of cancer. This product is the subject of this application for which approval is being sought.

Dated: August 19, 1997



Frank P. Hoffman
Associate Patent Counsel
Bristol-Myers Squibb Co.

Form OGD-011347 Revised 8/27/97
cc: Original NDA Division File

HFD-93 Mary Ann Holovac

HFD-1SD /D. Spillman
/Action Package

EXCLUSIVITY SUMMARY FOR NDA # 20-262

SUPPL # 024

Trade Name Taxol Injection

Generic Name (paclitaxel)

Applicant Name Bristol-Myers Squibb

HFD # 150

Approval Date If Known 6/30/98

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.

a) Is it an original NDA?

YES / /

NO / ✓ /

b) Is it an effectiveness supplement?

YES / ✓ /

NO / /

If yes, what type? (SE1, SE2, etc.)

SE 1

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES / ✓ /

NO / /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES / ☒ / NO / ☐ /

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

NOT SPECIFIED IN 12-17-97 SUBMISSION

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO-please indicate as such)

YES / ☐ / NO / ☒ /

If yes, NDA # _____.

Drug Name _____.

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

3. Is this drug product or indication a DESI upgrade?

YES / ☐ / NO / ☒ /

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved.

Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / ☒ /

NO / ☐ /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#	<u>20.262</u>	<u>Taxol</u>
NDA#	<u> </u>	<u> </u>
NDA#	<u> </u>	<u> </u>

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#	<u> </u>	<u> </u>
NDA#	<u> </u>	<u> </u>
NDA#	<u> </u>	<u> </u>

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES / ☒ / NO / ☐ /

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES / ☒ / NO / ☐ /

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not

independently support approval of the application?

YES / ☒ /

NO / ☐ /

PROJECT MANAGER
NOTE: see
12/17/97 +
~~6/12/97~~ BMS
Submission

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /☒/

If yes, explain: _____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /___/ NO /___/

If yes, explain: _____

(c) If the answers to (b) (1) and (b) (2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

① CA 139-165; ② CA 139-103; ③ CA 139-208

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

Investigation #3
If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /✓/

Investigation #2 YES /___/ NO /✓/

Investigation #3
If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

① CA 139-165

③ CA 139-208

② CA 139-103

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # _____ YES /___/

NO / ☒ / Explain: NOT sponsored IND, but NOT assigned rights to the data to the applicant under terms of a contract (CIADA)
See BMS letter of 12-17-97

Investigation #2

IND # _____ YES /___/

NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1

YES / ☒ / Explain See

BMS 12-17-97 letter

NO /___/ Explain _____

Investigation #2

YES /___/ Explain _____

NO /___/ Explain _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /☒/

If yes, explain: _____

/S/

Signature

Title: PROJECT MANAGER

June 18, 1998
Date

/S/

Signature of Office/
Division Director

6/30/98
Date

cc: Original NDA

Division File

HFD-85 Mary Ann Holovac

HFD-150 / D Spillman
/Action Package

(11)



DEPARTMENT OF HEALTH & HUMAN SERVICES

CSO Spillman
Public Health Service

Food and Drug Administration
Rockville MD 20857

Date JUL 25 1997

NDA No. 20-262

Bristol-Myers Squibb
Pharmaceutical Research Institute
5 Research Parkway, P.O. Box 5100
Wallingford, CT 06492-7600
Attention: Susan H. Behling, Assoc. Director
Worldwide Regulatory Affairs

Dear Sir/Madam:

We acknowledge receipt of your supplemental application for the following:

Name of Drug:	Taxol
NDA Number:	20-262
Supplement Number:	S - 024
Date of Supplement:	June 30, 1997
Date of Receipt:	June 30, 1997

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research, HFD-150
Attention: Document Control Room - 17B-20
5600 Fishers Lane
Rockville, MD 20857

[Signature]
Chief, Project Management Staff
Division of Oncology and Pulmonary
Drug Products